SIGMA XI QUARTERLY

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ANNOUNCEMENTS

The Executive Committee is privileged to present in this number of the QUARTERLY timely articles by three distinguished scientists. They will be read with interest by the nearly ten thousand members and associates of our great society to whom the issue is sent.

The annual convention of Sigma Xi will be held in New Orleans, Tuesday, December 29. The Executive Committee has the honor to announce that the tenth annual Sigma Xi address will be given by Dr. Clarence F. Hirshfeld, Director of Research of the Detroit Edison Company, member of our Alumni Committee.

President Stewart has appointed Professor C. E. McClung, University of Pennsylvania, Chairman of the Nominating Committee, which is to suggest officers for the ensuing biennium at the New Orleans convention. Chapters are asked to communicate their suggestions to Professor McClung direct, or through the office of the National Secretary. All recommendations will be given careful consideration by the Committee.

THE FUTURE MAN OF SCIENCE*

By G. W. Stewart, National President of Sigma Xi,
University of Iowa

We do not meet on an occasion when science is unjustly persecuted or hindered in its progress. It is not being prevented from playing an essential part in education. It is not being challenged as blasphemous. All that is past. On the contrary we find science today much favored, and more particularly in the respect and interest of the public. This respect has been fairly won, without resort to clever publicity, and chiefly by accomplishments that have been secured in a straight-forward, commendable endeavor. Science is respected as an intellectual effort of the highest order. It represents a process of thought that can be appreciated by the public, not because the content is readily understood, but because one can witness tangible results in the advancement of communication, transportation and all the innumerable conveniences in modern life, in electrical transmission of power, in all complicated inventions such as radio and television, in our atomic and astronomical knowledge and in our gradual, though entirely too slow, progress toward the prevention of disease and malignant disorders. In fact, so great is the public's interest and faith that a leading newspaper will publish verbatim, by cable, a most profound mathematical paper of Einstein, the only purpose being to enable the people to stare at the contribution and be profoundly impressed. An enthusiastic supporter of Wesleyan University purchased the original manuscript of this famous article for that institution. Among other evidences of the high respect in which Einstein is held as a thinker is that he recently received $25,000 for three pieces of parchment containing his statement of the present status of the theory of relativity. This record has been presented to Yale University. Has anything even comparable to this ever transpired? It is not satisfactory to reply that Einstein has been made a newspaper figure and that therein is the explanation. It is much more conservative to claim that there exists in this case today something bordering on an intellectual worship not only by experts but by the thoughtful people of this and other nations. The facts cited are really new in significance as well as in fact. For has not the appreciation of Einstein arisen out of the

* An address at the installation banquet of the Harvard Chapter.

background of widespread recognition of the accomplishments of science?

But the end of accomplishment in science is not in sight. It may appear that the chief branches of the fundamental sciences have been discovered and fairly well explored, and that ere long we will approach a saturation point of productivity, there remaining only the application in other fields such as medicine, engineering and more broadly in industry. But this cannot be true, for science has a definite appeal for its own sake. It has a distinct æsthetic value. It has a challenge to the human mind that will always attract those of high intellectual ability. Moreover, its history of successful attainment will continue to win future research workers. And superimposed upon all this inevitable interest in science is the possibility of new discoveries yet undreamed. No, there may be a diminution in the rapidity of the growth of science, but never in the prosperous development of science itself.

The influence of science will not depend entirely upon its laudation by the public and upon its continued growth and mastery over nature. Additional prestige will be obtained from the fact that in all fields of learning students are attempting to use the scientific method in creative scholarship. Everywhere we find a new stamp for intellectual goods, "Produced by the scientific method." This is in itself an admission that science, its attitude of mind and its process of thinking, are becoming more and more influential. It is not that this process of thinking belongs only to science. In reality it is very old. The novelty is chiefly the emphasis upon the importance of applying consecutive thought not only to the apparently significant practical problems in matter, but to the insignificant and more abstract ones as well. For example, the differentiation between magnetism and an electric charge was not made for at least twenty-one centuries after the simple basic experiments were known. These are the attraction of lodestone for iron and rubbed amber for light particles. It is not the process of thinking that is relatively new, but the confidence in its application to all subjects wherein the significant facts can be ascertained. Now what is the net result of the confidence in the scientific method? Science, by its support from the public and the wide adoption of its methods among numerous scholars in non-scientific fields, may, in a peculiar sense, and perhaps to too high a degree, dominate the highest type of education as found in our Graduate Schools. More than any

other division of learning it may determine the attitude of mind of the thoughtful people everywhere. I hesitate to make the prophecy too definite or too emphatic. But already the indications of its correctness seem strong. Even now it may be said that science is probably shaping the fundamental thought of men concerning life in both its emotional and intellectual aspects more than are the humanities. Even if this be an overstatement of the present conditions we have much right to have confidence in it as prophecy. If the prophecy be correct even in part, what a serious responsibility is thrust upon the future men of science!! Can and will they meet it? A moment's thought will show that our activities in science, though inspiring confidence of the thinking world in the leadership of science, have not saved us from our own narrowness.

At the installation exercises this afternoon the value of the chapter in an interchange of thought among scientific men was emphasized. This value need not be reviewed. Suffice it to say that the chapter's influence will be a distinct advantage in the cultivation of broad views and in making the possible future responsibilities of science more easy to carry.

It may be appropriate in conclusion to call attention to several directions of desirable improvement. Time will not permit a detailed discussion of them. I refer first to activity in the criticism of the misuses of the scientific method. Many are evidently fully aware of its inherent limitations and of the necessity of adequate confirmation of all conclusions.

The second opportunity is that we make the world conscious of the nature of the truth obtained by science. Our findings are frequently given too much confidence. The public prefers to assume that there is such a thing as absolute truth, and by inference, that science can and does ascertain fragments of it. But this is just what is not true. All of our discovered "laws" are not truths but only approximations.

The third suggestion is the recognition that, after all, science has a significant value only to man himself. This value cannot be measured accurately. It is somewhat vague. It stands upon precisely the same footing as the human values found in the history and literature of the many centuries past. The scientists must join with others in not only recognizing the value of the humanities but also in encouraging them actively.

The fourth opportunity arises in that the very success of science

puffs us up beyond all reason. The credit is due to the method and not to the scientists. Yet, because of our bigotry we can at times hardly restrain ourselves from giving public utterance to speculations based upon experiments, that, when read by the public, are destructive of certain human values. As an example of our mental danger notice how the microscope has prejudiced our minds. We look into a living cell with its complicated organism. We use a higher magnifying power and we see more. We may become convinced that if we had only a high enough magnifying power we could see life itself—that is, we could explain it. The truth is, we ought to know better. We do not know today precisely why molecules organize as they do and it is certainly not by peering through a microscope we will ever understand this ability of organization. The scientist of the future must be more basic in his views and should not expect to find life or anything fundamental except through a basic study of the most exacting character.

The purpose of these remarks is to call attention to the inevitableness of the growth, the development and the public appreciation of science, and to ask you to consider the future probable responsibilities and associated duties of the man of science. In this greater horizon for science I trust that Sigma Xi will play no inconsiderable part. By its association of men in different fields, it will both broaden and deepen the labors and thought of scientific men. It will make more clear to all of us the greater responsibilities of men of science and yet will, at the same time, issue a constant challenge to the highest quality of specialized creative scholarship of which man is capable. Whether or not my view of the future unsought opportunities of science is correct, Sigma Xi is an organization capable of assisting in any situation. Speaking for the Society again, I congratulate the University, and its spokesman, President Lowell, upon the potentiality of this new Chapter. And I congratulate the Society for this distinguished addition to its strength and usefulness.

UNIVERSITY STEPPING-STONES

By Dugald C. Jackson, Massachusetts Institute of Technology

A fund of facts, a creative mind, readiness to labor are features of the man who moves the world—the man of service. The earliest universities were made by such men in germ gathering as students around central men of fertile ideas to absorb from such ones, and each other, some facts, some inspiration to original thought, and some practice in developing creative ideas. Scholarship in the Middle Ages of Europe crystallized the scope of subjects then appropriate to university treatment. These comprised substantially all knowledge and fancy of the period, but excluded, because they did not then exist, all of those many branches of learning that sprouted rapidly after the opening of the Seventeenth Century, came to flower in the Eighteenth and Nineteenth Centuries and then through fruition produced many variant branches of importance during the first third of the Twentieth Century. The result ever since has been a continuous struggle to get into University circles by new branches standing outside of the inflexible University breastworks and resistance by those within against such invasion.

Youths aspiring toward the new learning, like electrons expelled from excited atoms, made a current outward. Conservatism within set up space charges opposing intruders. Philosophy, Theology, Mathematics, and the classical languages, originally within the breastworks, consorted contentedly with Astrology and Alchemy without a thought of the inadequacy of these pseudo sciences. Empirical and deductive thought entrenched themselves against competitors. Law and politics were welcomed within the walls, perhaps, because of their relation to philosophy. Branches of learning involving exact experimental observations associated with philosophical reflections about relationships of discovered facts were unwelcome. Seekers after inductive learning were compelled to battle for establishment of their subjects within the walls or turn to the recourse of establishing independent centers for securing their instruction. By means only of constant contest have the natural sciences like Physics, Chemistry, Biology, and Psychology won their present general acceptance in university circles.

Studies in modern history and modern languages came in by the same militant path, and are still sometimes treated as suspicious

characters. The modern applied sciences and the modern economics which relate to present-day business associations seemingly were peculiarly abhorrent to those who endorse limitation of universities to certain fields of learning instead of to levels of achievement, the abhorrence apparently being aroused because learning in the applied sciences and modern economics might become immediately useful and their followers might perchance profit in the pocketbook from such learning, it being argued that the chance for such profit is sure to neutralize intellectual profit. This disdain of the pocketbook when applied to the applied sciences and modern economics disregarded a like result arising out of the study of law which had become a cherished university branch. Thus it was illustrated that to the philosopher exact logic presents no restraints unless it supports what he denominates his principles. And here we see that principles in philosophy are empirical; just as is true of the bases of mathematics, wherein we may assume the Euclidean axioms or cast off into some non-Euclidean realm at pleasure.

The study of applied sciences, agriculture, engineering, medicine, and their brothers, is now established in university circles after much battle. And so also is the study of modern economics which maneuvers on the borders of being a scientific entity. The acceptance is completely established in this country and to considerable degree in Great Britain and other European countries. Indeed, in this country it may be said of engineering education, that its logically coherent curricular programs set out in sufficient number of modifications to satisfy the intellectual tastes of students who choose to enter the field of engineering, associated with freedom of election by substitution for the benefit of individuals who have reached sufficient maturity to demonstrate fitness for making their own case, ever have been a steadying and rectifying influence in national higher education.

Having been accepted the medical schools have cut out their special field in the university world and invite within their borders only those who have had special preparatory education. Agriculture looks somewhat askance at its acceptance as a branch of university learning and holds somewhat aloof, perhaps on the unsound thesis that a tiller of the soil is solely a man of the soil and not a man of dreams.

Engineering has more closely articulated into the general university setting. The older scholars there find it hard to remember that

modern applications of science and economic philosophy are the influential humanities of today and tomorrow and perhaps the future, and also perhaps these older scholars may feel a little resentful to have injected into the midst of their scholarly circles the pragmatic-minded engineers who have been granted equal intellectual rights with their own, since this phenomenon tends to break down artificially imposed older tests for scholarly endeavor. However, a successful engineer usually must be a cultured man of the world, and the engineering schools therefore find co-operation with the oldtime scholarship desirable in aiding their neophytes in preparing themselves for activity in the engineering field. We perhaps do not see very clearly how this co-operation may be best established or how deep it should go. We probably are as awkward about it as our associates who embrace the older branches of learning. But I believe that we are all sincere in approval.

Perhaps our awkwardness is partly due to an embarrassment caused by a different emphasis on the sense of responsibility. The philosopher may have no urge to carry an interesting conception through to a logical issue and thus subject his reasoning to pragmatic tests. The conception and its immediate corollaries may define the limits of his interest, and none may criticise him for there leaving the pursuit. A reputable investigator in science may turn aside from any investigation without justifying criticism from any one, when the vista ceases to inspire him to further efforts; and that regardless of the presence or absence of promise of fruitfulness from research continued along the same path extended. Even the classical economist feels no obvious professional sense of responsibility for the soundness of his ideas or the applicability of his premises in existing social conditions. For example, the economic premises formulated by Adam Smith were drawn out of his observations of the economic state in his day. A century and a half later the state of organized society does not test according to his premises unmodified, and it is, therefore, only fanciful to attempt to apply his unmodified conclusions to our present civilization, although this often is done.

The engineers have further responsibilities imposed upon them, whether they are associated with university faculties or not. They have responsibility for carrying through to conclusions and then testing the conclusions pragmatically by comparison with events. Along with our university colleagues in various branches, we know that the exertions accompanying conception are sweet; but after

conception (as a colleague has put it) for us comes labor, or the conception fails in fruit. In this scientific age the wastes of sweetness and light due to delays in making serviceable applications of knowledge are too grave to be endured with equanimity and this makes the responsibility heavier and more important. When a philosophy is cast into the dump of useless doctrines because it no longer works, it does no good to fish it out, weep over it and try to refurbish it. The path to truth is attained by facing facts as they are, and endeavoring to establish the structure of a doctrine which can stand the test of all facts, whether they are of hoary age or recently observed.

A creative mind is one with the power of seeing new things. It reasons truly and justly. It dreams concrete dreams. It investigates. Such a mind is creative equally whether its possessor chooses a field where conception may be laid before the world and responsibility for final achievement be left for others to take up, or the possessor chooses a field where conception and application are more closely linked. Both types of creative mind are sadly needed in this world, and equal honor should be accorded their creative powers. John Ruskin remarks that "Hundreds of people can talk for one who can think; but thousands can think for one who can see." Such unique people, who can see, in my opinion are appropriate to the highest order of university life; and I believe that most members of university circles will agree with that opinion. With this assumption I shall proceed to illustrate somewhat more concretely the place of engineering in university life.

Engineering in the universities is the field of the economic applications of the forces of nature. It utilizes and overlaps with applied mathematics, mathematical physics, experimental physics, chemistry, biology, and economics, and includes on one border a range of engineering applications which involve natural forces and their interrelations that are capable of being dealt with rigorously or as a group of investigatory subjects branching from the main stem. On the other border lie those engineering achievements which are primarily a response to economic pressure, and which involve physical interrelationships in such complex manner that analysis cannot be complete until our intellectual powers are extended beyond their present scope. The development of these interrelationships ought to be subjected to more rigorous analysis and clear exposition. A comprehensive region between the border which overlaps into the

sciences and the border which overlaps into economics contains an infinitude of problems in which the aspects of the two border lands are closely interwoven. The field of engineering thus overlaps the fields of mathematics, physics, chemistry, biology, and economics, just (for example) as the fields of mathematics and physics dovetail into each other as well as into the field of engineering.

It is impracticable to successfully work in the middle portion of the field of engineering without also cultivating the border parts, and work in the portions overlapping other subjects may be done by men of achievement either in the engineering departments or by men of like achievement in adjacent departments, or by both without just jealousies on either side. In fact, co-operation is advantageous to all sides working in overlapping situations.

Creative engineers in this era must be scientists by education and intellectual qualities. The same is gradually becoming to be true of the creative men even in the administrative aspects of the engineering industries. But the human, economic demands on engineering require other intellectual qualities added to those of a scientist solely. Under university conditions the engineering staff must be scholarly scientists. Some must be primarily interested and effectively occupied in experimental and mathematical research in physical phenomena. All must be apt in knowledge of economics and the engineering requirements respecting useful applications of science, and some must prefer specific mastery in this side of the field.

The intimacy between pure science and engineering science cannot be overemphasized. However, certain distinctions also exist which may be made clear by examples, thus: The disclosure and mathematical exposition of the modes of vibration of a loaded string by Lagrange was a scientific achievement of high order and made an addition to organized knowledge, *i. e.*, to science. But it required equally high additional achievements in engineering by Pupin, Campbell, and Jewett to establish the analogue in electric circuits as a powerful instrument for the extension of economical telephonic transmission. The discovery and disclosure of the qualities of complex quantities in higher algebra by Wallis, Wessel and Argand composed an achievement of higher order in science, but it required the scholarly engineering intelligence of Steinmetz and others to establish the appreciation of complex quantities as the powerful instrument for solving problems of electromagnetic circuits and machines which they now are. The basic principles of thermionics

and the conduction of electricity through gases at low pressure has been a favorite research ground for physicists, but it required the impetus and co-operation of scholarly engineering vision and intelligence to bring to pass the extraordinary rectifiers of large capacity that now are making a sensation in electrical engineering. Musical vibrations and the vibrations of reeds and diaphragms were subjected to important scientific investigations and discoveries by Helmholtz and Lord Rayleigh, but it took the engineering intelligence of men of the type of Timoshenko and Hovgaard to show the applications of the same laws of vibrations to operating characteristics in man-made machines.

It is not necessary to go on multiplying examples. In this age it is deemed an economic waste to allow to lie on the shelf any science that engineering intelligence can convert to useful purposes. Success in producing men with the powers of intelligent synthesis which this demands has endeared the engineering schools to the American people and is a cause of their uniquely high standing in popular estimation.

The engineering departments of our great educational institutions are well established and should continue to expand their creative work in the borderland which overlaps with the mathematics, physics, and biology. They also work intensively, but are not equally well established, in the borderland which overlaps with economics. The latter borderland—contrasted with studying, investigating, and guiding phenomena of nature related to physical phenomena—consists in studying, investigating, and guiding the economic and social uses of structures, power, machinery, communication of intelligence, transportation, and the influence of engineering on modes and conveniences of life. We have a good start in this, but with less intensive cultivation than on the mathematical-physics side. The appropriate manner of carrying on is by statistical and scientific investigation to establish facts and relations that are now perceived only dimly or perhaps not yet perceived at all. This co-operation should be and can be as fully established as on the mathematics-physics border. The object is to place this economics side of engineering on the same altitude of rigorous examination and reasoning as now characterizes the science side of engineering in the engineering schools, while scrupulously avoiding detracting from the progress of the latter. Collaterally, the object is to develop more rigorous investigation in this now neglected or only loosely studied field.

Besides leading their students to familiarity with the tenets of science and economics the engineering staffs have the additional obligation to translate to the students a scholarly engineering vision of the principles of science and economics embodied in the works of man wrought in materials such as metals, stone, wood, and fibre, and the influence on civilization which is concomitant to those embodiments. "Machines, the slaves begotten of man's thoughts" have done us relative good, but until the articulation of engineering into economics is worked out in the engineering schools of university rank as fully as the articulation which now exists with mathematics, physics, chemistry, and biology there will be danger of the relative good becoming relative evil. I do not charge this fault to the economists, theirs being a philosophical field; but we, the engineers, must bring to pass a co-operation which joins our scientific, pragmatic attitude to their philosophic tendency. From such co-operation brought to pass in engineering schools of high level, we may validly hope for the solution of such perplexing problems, for example, as the periodic recurrence of acute unemployment, and the ultimate formulation of effective means for prevention.

When the engineering departments have accomplished this co-operation in the institutions of university level and have secured a communion with the economists of a level and order equal to our communion with the scientists, we will have established our buttresses in both sides of the field and will be in position to most serviceably cultivate the full area. It is a fairy book which is coming to realization.

RECENT ADVANCES IN ENZYME CHEMISTRY; THE MECHANISM OF PEPTIDE-HYDROLYSIS

ARNOLD K. BALLS, UNIVERSITY OF PRAGUE, CZECHOSLOVAKIA

You have often heard that active living tissue is in a constant state of chemical change, and that an untold number of chemical reactions are taking place within and around it. Many of these reactions occur with great rapidity, because the living cells elaborate substances which have the power to hasten, that is, to catalyze them. These substances are the enzymes, or ferments; and they are true catalysts in that they can only accelerate a reaction which would otherwise take place, though slowly, while they cannot start a reaction going which would otherwise not occur at all. Spongy platinum, as you know, when introduced into a mixture of oxygen and hydrogen, or into a solution of hydrogen peroxide, is an example of an inorganic catalyst. The enzymes, or ferments, if you care to call them so, are on the other hand organic substances, elaborated by the living cells, which catalyze the chemical changes occurring in and round living matter.

The action of these ferments is in one sense difficult to investigate. Although we have evidence to show that they are definite chemical substances, they have never been isolated, except in two instances as crystalline proteins, and our knowledge of proteins is so meagre that this does not help much. In most cases we cannot be sure that the enzymes even belong to any of the well-defined classes of biological substances, such as the proteins, carbohydrates, or fats. Furthermore, they occur in nature in exceedingly small amounts, and it would require enormous quantities of material to obtain enough of the pure ferment to work with; to make matters worse, the enzymes are all soluble in water, and they are very unstable. Their activity often disappears if you try to purify them. Apparently, the ferments cannot exist alone in solution; some protective colloid must always accompany them, perhaps in a sort of combination, similar, it has been suggested, to the combination between the colored substance hemin and the protein globin as they exist in hemoglobin.[1]

So you see that there is a reason why enzyme chemistry is still in its infancy. In the face of these difficulties, it may seem a bit adventurous to ask ourselves the question: What chemical processes

underlie what we term enzyme action? How does it take place? Given the system enzyme-substrate, what happens between these two before the substrate actually appears in the digested condition? In other words, what is the mechanism of an enzymic process?

Nobody could pretend to really answer this question today, but I think there has nevertheless been a start made toward its solution. I do not need to comment on the importance of this question to the theoretical biologist, but it has a practical side as well. The fact that the ferments are able to function after being separated from their parent cells, makes them valuable chemical reagents in medicine, in industry, and in research. For example, consider the tremendous blood-clotting power of tryptic proteinase,[2] or the long list of industrial fermentations, at the basis of each of which lies an enzyme reaction, or the recent work on the composition of the protamines,[3] and the newly developed structural formulas for sugars and glucosides[4] in an ever-increasing number.

This question of the mechanism of an enzymic process would, however, be a pretty hopeless one, if it were not for one fact, that many of the chemical reactions occurring in and round living tissue are quite well-known and defined, they may be repeated in the laboratory with dead material, and most important of all, with synthetic chemicals. Under such circumstances, the enzymes are still able to hasten the speed with which the reactions occur.

This acceleration is sometimes very marked. Perhaps the most effective enzyme preparations ever made were certain catalase preparations of v. Euler and Josephson.[5] Catalase is an enzyme which, like spongy platinum, decomposes hydrogen peroxide into water and oxygen; and these preparations were able to decompose the enormous quantity of about thirteen thousand times their weight of hydrogen peroxide per minute.

But even more curious than the rapidity of enzyme action, is its specificity. An enzyme seems able to catalyze one particular reaction, and absolutely no others. The effect is therefore confined to some particular group of substances, sometimes to only one known substance. It is this specificity of action which has finally given us a clue to the mechanism by which the enzyme performs its catalysis. It is, as you will see, not only the last court of appeal in experimentation, but also the underlying matter of thought at the base of everything which I have to say to you tonight.

The nature of enzyme action was bound to remain unexplained

until Willstätter showed us how to obtain preparations of a single enzyme, instead of the old mixtures containing several.[6] The headway thus gained seems to have led to a few fundamental principles which underlie the whole field. It is therefore not quite fair to assert that by studying one enzyme, one learns nothing about the others. On the contrary, we probably learn much more than we are yet able to appreciate. It is not, therefore, because the peptidases possess any overweening importance as ferments in the biological economy, that I wish to discuss them this evening, but rather because our relatively greater knowledge of them is important to the whole field of enzyme research.

Now, the most frequently observed reaction in biological chemistry consists in the transfer of water from one molecular configuration to another. That is, a hydration or a dehydration process, depending upon which side of the chemical equation you have in mind. The digestion of the proteins, for example, is chemically an hydrolysis, and is accelerated by the presence of the proteolytic enzymes. You will remember that the protein molecule is composed of long chains of amino-acids. These chains are called peptides, and the amino-acids composing them are all joined together in the same way. Take the formula of the simplest amino-acid, glycine:

$$NH_2—CH_2—COOH$$

You will note that on one end is a free NH_2 or amino group, while on the other end there is a carboxyl, or acid group. Now Emil Fischer has taught us that the amino-acids are joined together in the proteins in this way:

$$NH_2—CH_2—CO\,\ddot{O}H + H\,NH—CH_2—COOH \longrightarrow NH_2{\cdot}CH_2CO—NHCH_2COOH + H_2O$$

diglycine

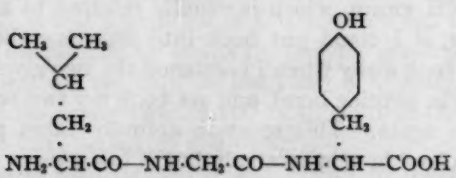
From two molecules of glycine, one molecule of the dipeptide diglycine is formed, and one molecule of water is split off. The same process could be repeated to form a tri-peptide, or a tetra-peptide, and Abderhalden[7] has made a peptide containing nineteen amino-acids in one chain. The linkage between the amino-acids is, as you see, the CO–NH group, which is usually referred to as the peptide linkage. Now, if I could put back into diglycine the molecule of water which I took away when I combined the two glycines together, I should split the peptide bond, and get back my two original amino-acid molecules again. This reaction actually takes place when a peptide is dissolved in acid or alkali, but it takes place slowly. It is

the function of the proteolytic ferments to speed up this reaction. The proteinases are therefore referred to as splitting, or hydrolyzing, or even digesting, the huge protein molecule down to the polypeptide stage. The peptidases complete the process by accelerating the decomposition of the polypeptides down to their constituent amino-acids. And these amino-acids are adsorbed by the organism as nutriment. Perhaps there is another group of enzymes which assist in breaking down the most complicated polypeptides into the simpler ones, but this cannot be stated definitely today.

The substrate of the enzyme is the substance whose decomposition the enzyme accelerates. The substrates of the peptidases are naturally the peptides. You are perhaps familiar with the work of Michaelis[8] and that of Nelson[9] on invertin, or with its counterpart on the peptidases by Waldschmidt-Leitz and von Schuckmann,[10] upon which is based the assertion that the first step in enzyme catalysis is the formation of a chemical compound between the ferment and its substrate. I think that this thesis would meet with very little opposition today, and I do not wish to discuss the fact that such a combination takes place, but rather to consider in some detail what sort of a combination this is.

It was Northrop[11] who pointed out that the proteinases differed from each other in the way by which they combined with their substrates, the proteins. A protein may, as you know, exist in solution either as an acid, or as a base, or as a neutral molecule. Pepsin combines with the basic protein form, or protein cation;[11] trypsin, that is, tryptic proteinase, appears to combine with the acid protein form, the protein anion,[12] although here the evidence is not so clear. Later Willstätter pointed out that a third group of enzymes, the papaïnases (the type comes from *carica papaïa*), were able to combine with the isoelectric protein, that is, with the electrically neutral protein molecules.[13]

The state of affairs in the case of peptidases is quite similar, as Waldschmidt-Leitz has shown. In order to make this clear I will write the formula of a simple tri-peptide, leucyl-glycyl-tyrosine.



You will note that on one end of the peptide chain there is a free NH_2 and on the other end, a free COOH group, just as is the case with the amino-acid. There are a number of peptidases which combine with the acid group of the peptide, the COOH group, just as there is a proteinase which attaches itself to the acid protein molecule. These peptidases are naturally called carboxy-peptidases.[14] On the other hand, the amino-peptidases[15] combine with the free amino group at the other end of the peptide chain.

The recent work in this field by Waldschmidt-Leitz has shown that erepsin and trypsin, which were formerly regarded as single enzymes, are by no means so easily disposed of. They are not single enzymes, but complicated mixtures of several ferments, whose relative proportions can vary greatly.[14-16] Now that pepsin has been crystallized by Northrop,[17] I am waiting with great curiosity to see whether the integrity of this enzyme may not also be questioned. On the other hand, the so-called rennin, supposed at one time to be the partner of pepsin in the stomach, is nothing more than another manifestation of pepsin itself.[18] So that, if modern research has increased the number of enzymes here and there, it has also succeeded in discarding others.

The proteolytic system of the pancreas and intestine may now be described as follows:

Pancreas (trypsin)	a proteinase attacking protein anions—tryptic proteinase a carboxy-polypeptidase attacking polypeptides from the COOH end
Intestine (erepsin)	an amino-polypeptidase attacking polypeptides from the NH_2 end a dipeptidase attacking dipeptides only, also from the NH_2 end

The method of deciding which group of the peptide combines with the enzyme is very simple, once you have the enzyme free from admixture with other ferments. One selects a digestible peptide, such as the leucyl-glycyl-tyrosine mentioned above, and then one studies the action of the ferment upon the derivatives of this peptide. The amino-polypeptidase splits not only the original peptide, but also all of its derivatives in which the free amino-group has been left intact. Furthermore, it will split none of the derivatives in which the amino group has been modified or removed. As examples, the peptide ester is split, but the acetylated peptide remains unattacked. The exact reverse is true of the carboxy-polypeptidase. This cannot split the ester, but attacks the acetyl derivative. It seems, therefore, reasonable to conclude that the compound formation with the

ferment, which is known to occur in any case, does so between the ferment and the particular group of the peptide, without which the enzyme is unable to function.

peptide:	NH_2-leucyl-glycyl-tyrosine-COOH	Split by amino- and by carboxy-polypeptidase
peptide-ester:	NH_2-leucyl-glycyl-tyrosine-$COOC_2H_5$	Split by amino-, not by carboxy-polypeptidase
acetylated peptide:	CH_3CONH-leucyl-glycyl-tyrosine-COOH	Split by carboxy-, not by amino-polypeptidase

Only one amino-acid may be split off at a time by either the amino- or the carboxy-polypeptidase, and this amino-acid is the one at that end of the peptide chain which the enzyme attacks.[19] In this way, the peptide is gradually whittled down, from one end or the other, until a dipeptide is all that is left. Here the action of the polypeptidases ceases, and the dipeptidase finishes the process by splitting the dipeptide into its two constituent amino-acids. After this fashion the entire protein molecule containing 300 or 500 or perhaps 600 amino-acids, is completely broken down into those same amino-acids, from which it was once-upon-a-time built up a living cell.

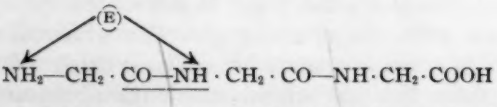
We think in Prag that we have also found the peptidase counterpart of the papaïn type of proteinase, namely, an enzyme which combines with neither carboxyl nor amino groups, because it splits substances which contain none.[20] For example, chlor-acetyl-ortho-nitraniline, is split by this ferment, and it seems fair to assume that it combines with the peptide linkage itself. That this assumption is not entirely without parallel, I hope to show you in a few minutes.

The foregoing constitutes the basis of our present ideas regarding the mechanism of peptidase action, and it is quite definite and well substantiated, as far as it goes. But it does not go far enough to explain why some peptides we know are not split. Take, for example, the decomposition of the peptide glycyl-leucine. This peptide exists in two optical modifications, glycyl-l-leucine, and glycyl-d-leucine. Glycyl-l-leucine is split by the dipeptidase of the intestine, which first combines with the free amino group of the glycine. Glycyl-d-leucine is not split. If nothing more than the compound formation between the enzyme and the amino group were needed to bring about the decomposition of the peptide, then as long as this contained its free amino group, it ought to be split

by the ferment. Long ago, Emil Fischer showed that this was not the case.[21] But this really means that the constitution, or the configuration of the second component amino-acid of the peptide is just as important in determining its digestibility, as is the constitution of the first component, with which the enzyme is known to combine. If I take the case of a polypeptide, say glycyl-leucyl-tyrosine, not only must the first component—the glycine—have a free amino group, but the second component must be lævo leucine, and not dextro leucine. On the other hand, the third component, the tyrosine, seems to be so far removed from the sphere of action of the enzyme, that it has no influence. It may be either l or d tyrosine, without affecting the scission of the glycine from the other end. How does it happen that the enzyme which combines with the first component, is nevertheless so completely at the mercy of the second component, but cares nothing at all about the third?

The answer to this question may be, as Abderhalden[22] has suggested, that the peptide linkage of the entire enzyme-substrate compound possesses a different degree of stability toward the solution in which it is dissolved, from that possessed by the peptide itself. In other words, the stability of the peptide bond is modified by the presence of the enzyme within the molecular complex. I should like to offer for your consideration tonight an idea regarding how this modification of the stability is brought about.

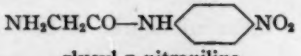
As a matter of speculation, the view is by no means novel, that the enzyme not only unites with its substrate through the active groups which I have just described (here the free amino group), but that it also unites with the substrate a second time, and with a second active group in the substrate molecule. This was first proposed by von Euler and his collaborator, Josephson,[23] to explain the mode of action of yeast invertin. But the theory is particularly intriguing when applied to the peptidases, when one assumes that by combining a second time with the substrate, the enzyme straddles the peptide bond which is later to be torn apart.



It is easily seen that the amino-acid on the other side of the peptide linkage may also have its own requirements for combining with the enzyme, and that these will also determine, just as definitely as the

presence or absence of a free amino group, whether or not the peptide will be split. The third amino-acid of the chain will, however, have no part in this reaction.

The question might well be raised at this juncture: with what second group in the peptide molecule can the enzyme combine? To answer this, it is necessary to consider the behavior of some of the synthetic substrates. You have seen that the simple peptides are in one sense much alike. They all have an amino group at one end, a carboxyl group at the other, while in between is a row of peptide linkages. In the laboratory, however, peptide-like substances may be synthesized to correspond to almost every condition which it may be desired to investigate. It is remarkable that such a large number of these unnatural substrates are split by the peptidases, although their resemblance to a peptide is often largely a matter of tacit courtesy on the part of the audience. For example, glycyl-para-nitraniline is easily split by the intestinal dipeptidase.[24]



glycyl-p-nitraniline

This fact is not only a proof of the assertion that the dipeptidase requires no carboxyl group, but it also points out that the second active group of the substrate must reside in the peptide linkage itself. There is in fact no other available point of attachment.

The list of aniline derivatives which react with the dipeptidase may easily be lengthened until it contains quite a number of substances.

Split	Not split
glycyl-p-nitraniline	glycyl-aniline
glycyl-p-amino-benzoic acid	glycyl-o-toluidine
glycyl-m-amino-benzoic acid	glycyl-p-toluidine
glycyl-p-nitraniline-o-carboxylic acid	glycyl-o-amino-benzoic acid

Note here the case of glycyl-aniline as opposed to glycyl-nitraniline, and that glycyl-ortho-amino-benzoic acid is not decomposed, while both glycyl-meta- and glycyl-para-amino-benzoic acids are digested. You see also that if a nitro group is introduced into glycyl-ortho-amino-benzoic acid, the resulting glycyl-para-nitraniline-ortho-carboxylic acid is again decomposable. The behavior of these aniline derivatives shows that the second combination between the enzyme and substrate can only occur when the NH of the peptide linkage possesses a certain acidity level. This acidity level has been obtained in the examples shown by the introduction of a nitro group

into the benzol ring. The introduction of more carboxyl groups produces the same effect, and in the natural peptides it is the nearness of the carboxyl group which gives the peptide linkage the acid character necessary to allow its combination with the enzyme.

This combination takes place, in all probability, between the enzyme and the imino group of the peptide linkage. In fact, by substituting the imino hydrogen of the peptide linkage by an acetyl group, Bergmann, DuVigneaud, and Zervas have prepared peptide derivatives which decompose spontaneously in water.[25] Here the acetyl group modifies the stability of the peptide bond very much as I picture the enzyme to do.

If this theory of the mechanism of peptide decomposition be true, then the enzyme, prior to the hydrolysis of the peptide, is bound to its substrate in two places, one on each side of the peptide bond. The two haptophore groups of the peptide are the free amino (or carboxyl) group of the first component amino-acid, and the imino group of the adjoining peptide linkage. The splitting of the substrate can only occur when the acid character of the imino group is sufficiently pronounced to permit of compound formation between it and the enzyme.[26]

You will have noted that the basis for this explanation is, however, an assumption, namely, that the above-mentioned compound formation actually does take place. The evidence for this is, from the nature of the case, indirect. The probability of the explanation is greatly increased, however, by evidence which, though again indirect, is obtained by an entirely independent method, and which also tends to show that a compound formation between the imino group and the ferment takes place. This evidence comes from what may be called inhibition experiments.[27]

If I blockade the amino group of a peptide, by introducing into it an acid radical, such as acetyl or benzoyl, I obtain a substance which is no longer split by the amino-peptidases. Nevertheless, this substance still contains a peptide bond, whose acid character, due to the neighboring acid group which I have introduced ought to be high enough to fulfil the conditions of this theory. Such a substance should still be able to combine with the enzyme. The enzyme so combined, that is, on the imino group of the new substance, would no longer be able to combine with, and to split, a really digestible substrate. The result of this situation would be, that as part of the enzyme present is withdrawn from active service, one could expect

to observe an inhibition of the enzyme action, produced by the presence of the new substance.

This is exactly what happens. If the amino-polypeptidase is catalyzing the decomposition of a polypeptide, and acetyl-diglycine or benzoyl-diglycine is added to the system, the digestion is at once slowed up. If the carboxy-polypeptidase operates in the presence of chlor-acetyl-para-amino-phenol, its action is inhibited.

Now, in the first place, this inhibition of the ferment action is not what is called an enzyme poisoning, but it is based upon a reversible reaction between the ferment and the inhibiting substance. The substrate, which is digestible, and the inhibitor, which is not digestible, compete with each other for the possession of the enzyme. At any fixed concentrations of enzyme, substrate, and inhibiting substance, an equilibrium exists between the amount of enzyme combined with the substrate, and the amount combined with the inhibitor. Any change in the proportion of these substances produces a corresponding change in the equilibrium. By adding more substrate, the proportion of the enzyme combined with the substrate is increased, and the digestion observed proceeds at an increased rate. If the amount of inhibitor is increased, more of the enzyme is removed from its compound with the substrate, and the rate of digestion is diminished. If the proportion of substrate and inhibitor is kept constant, then the fraction of enzyme combined with the inhibitor and that combined with the substrate always remains the same, no matter how much enzyme is present. This is the same situation as when two acids of different strengths compete for an excess of a base.

Secondly, it can be shown that the inhibition is caused by the terminal imino group of the peptide chain. That is, with the derivatives we have used, by the imino group adjacent to the introduced acid group. Compare the formulas of benzoyl-glycine, with one peptide bond, benzoyl-diglycine with two peptide bonds, and benzoyl-triglycine with three.

Benzoyl-glycine:	$C_6H_5CO—NH.CH_2COOH$
Benzoyl-diglycine:	$C_6H_5CO—NHCH_2CO—NHCH_2COOH$
Benzoyl-triglycine:	$C_6H_5CO—NHCH_2CO—NHCH_2CO—NHCH_2COOH$

Equimolecular amounts of these substances produce quantitatively the same amount of amino-polypeptidase inhibition. That is, the additional imino groups of the higher peptides do not react with the enzyme. This fits nicely with the observation that when a long

chain peptide is hydrolyzed, only one amino-acid is split off at a time.

TABLE I

INHIBITION OF AMINO-POLYPEPTIDASE BY EQUIVALENT AMOUNTS OF SUBSTITUTED PEPTIDES

Each determination consisted of 5 cc., containing, besides the substances shown below, 0.001 mol phosphate (as buffer) and 0.0005 mol leucyl-diglycine (as substrate). PH = 8.0. The amount of digestion was measured by titration in alcohol with *N*/5 KOH.

Inhibitor		Units of amino-polypeptidase	Time	Increase in acidity
None	....	0.0086	90	0.80
Brom-isocapronyl-glycine	0.0005 mol	0.0086	90	0.42
Brom-isocapronyl-diglycine	0.0005 mol	0.0086	90	0.44
Brom-isocapronyl-triglycine	0.0005 mol	0.0086	90	0.44
None	....	0.0148	60	0.89
Benzoyl-glycine	0.0005 mol	0.0148	60	0.24
Benzoyl-diglycine	0.0005 mol	0.0148	60	0.28
Benzoyl-triglycine	0.0005 mol	0.0148	60	0.21
None	....	0.0142	60	0.83
Benzoyl-sarcosine	0.0005 mol	0.0142	60	0.78

Thirdly, an experiment is possible which points directly to the hydrogen atom of the peptide linkage as the seat of this anchoring place for the enzyme. Benzoyl-glycine inhibits peptidase action very strongly. If I substitute the hydrogen of the imino group in benzoyl-glycine by a methyl group, I have benzoyl-sarcosine. I have taken away the imino hydrogen, and benzoyl-sarcosine is not capable of inhibiting the ferment action.

$C_6H_5CO—NHCH_2COOH$ benzoyl-glycine
$C_6H_5CO—N(CH_3)CH_2COOH$ benzoyl-sarcosine

These experiments appear to point to an important generalization, namely, that the peptidases possess in common the property of compound formation with an appropriately acid-imino group. On the other hand, their differences depend upon which of the other groups, amino or carboxyl, they are able to attack.

Accordingly, both the amino-polypeptidase and the dipeptidase should compete for the same inhibitory substance. This has been tried, and we have actually found that the inhibition of dipeptidase may be lessened, and indeed almost removed, by adding to the system some of the purified amino-polypeptidase, although the latter enzyme is absolutely unable to split the substrates of the dipeptidase. It is a case of the two peptidases competing for the same imino group in the benzoyl-glycine. I believe I am correct in saying that

this is the first similarity in the mechanism of action to be observed between the enzymes of any one general group.

TABLE II

ADDITION OF AMINO-POLYPEPTIDASE CAUSES A DECREASE IN THE INHIBITION OF DIPEPTIDASE BY BENZOYL-GLYCINE

Each determination (5 cc.) contained, besides the substances shown below, 0.001 mol phosphate (as buffer), 0.00033 units of dipeptidase (as erepsin), and 0.0005 mol leucyl-glycine (as substrate). Digestion determined by titration in alcohol after 180 min. at 30°. PH = 8.0.

Amino-poly. units	Benzoyl-glycine mols	Acidity increase cc. *N*/5 KOH
none	none	0.68
none	0.0005	0.25
0.0072	0.0005	0.41
0.0143	0.0005	0.47
0.0286	0.0005	0.49

On the foregoing experiments I hope to rest the case for the "two-affinities" theory of peptidase action. But this theory carries with it a number of interesting implications. Among them is a possible explanation of the difference between the dipeptidase and the amino-polypeptidase. Both are amino-peptidases, but one ferment splits only dipeptides, the other only polypeptides. Why should a chain of two amino-acids behave so differently from one of three, when a chain of three acts so similarly to one of four or five or ten?

If you will compare the formula of a dipeptide with that of a tri-peptide, you will see that the COOH group is very near to the reacting imino group in the dipeptide, while in the tripeptide it is much farther away. Let us assume that the combination of the enzyme with the amino group destroys, at least partly, the basicity of the latter. Then the imino group of the dipeptide, because it is so near the acid COOH, may well be more acid than the NH group which is attacked by the enzyme in the polypeptide. The dipeptide may therefore combine with an enzyme whose basic character is weaker. The dipeptidase could, therefore, be thought of as the weaker base. This would explain why the dipeptidase cannot split polypeptides. On the other hand, if the dipeptidase is to be considered the weaker base, then the polypeptidase is the weaker acid, and it might not be acid enough to combine with the free amino group of the dipeptide. The amino group of diglycine has recently been shown to be less basic than the corresponding group in triglycine.[23] This would explain why the polypeptidase cannot split dipeptides.

This deduction is actually born out by the behavior of these two enzymes toward free amino acids. The dipeptidase can combine with the free amino-group of an amino-acid (an old experiment of von Euler's), while the amino-polypeptidase cannot unite with so weakly basic a group as the NH_2 of glycine.

TABLE III

BEHAVIOR OF SOME AMINO-ACIDS TOWARD AMINO-POLYPEPTIDASE AND TOWARD DIPEPTIDASE

Besides the substances shown below, each determination contained (in 5 cc.) 0.001 mol phosphate and 0.0005 mol substrate. Digestion determined by alcoholic titration after 120 min. at 30°. PH = 8.0.

Amino-acid		Enzyme	Acidity increase cc. *N*/5 KOH
		Polypeptidase units/5 cc.	
none		0.0071	0.86
glycine	0.001 mol	0.0071	0.86
α-alanine	0.001 mol	0.0071	0.85
α-leucine	0.001 mol	0.0071	0.84
α-glutamic ac.	0.001 mol	0.0071	0.85
		Dipeptidase units/5 cc.	
none		0.0013	0.77
glycine	0.001 mol	0.0013	0.50
α-alanine	0.001 mol	0.0013	0.50
α-glutamic ac.	0.001 mol	0.0013	0.38

The "two-affinities" theory of peptidase action has, it seems to me, justified itself as a working hypothesis, and it appears to explain what is known of the effects, and particularly of the specificity, of the peptide-splitting ferments. It is supported by independent evidence pointing to a general reaction between the peptidases and one of the imino groups in their substrates.

To repeat what I said before, it may seem a bit adventurous to ask ourselves the question: What is the mechanism of an enzymic process? Nobody could pretend to really answer this question today, but I still believe that there has been a start made toward its solution.

REFERENCES

[1] R. Willstätter: Faraday lecture, *Jour. Chem. Soc.* 1927, p. 1359.
[2] E. Waldschmidt-Leitz, P. Stadtler, and F. Steigerwaldt: *Zeits. physiol. Chem.* 183, 39 (1929).
[3] A. Schäffner: Enzyme und ihre Bedeutung zur Konstitutions-ermittlung von Naturstoffen. Berlin, 1930.
[4] E. Waldschmidt-Leitz, A. Schäffner, and W. Grassmann: *Zeits. physiol. Chem.* 156, 68 (1926).

[5] H. v. Euler and K. Josephson: *Ann. Chem.* **455,** 111 (1927).
[6] R. Willstätter: Untersuchungen über Enzyme. Vol. I, p. 66. Berlin, 1928.
[7] E. Abderhalden and E. Schwab: *Fermentforschung* **10,** 179 (1928).
[8] L. Michaelis and E. Menten: *Biochem. Zeits.* **49,** 333 (1913). L. Michaelis: *Ibid.* **115,** 269 (1921).
[9] J. M. Nelson: *Jour. Amer. Chem. Soc.* **39,** 790 (1917); **50,** 2188 (1928).
[10] E. Waldschmidt-Leitz and G. v. Schuckmann: *Zeits. physiol. Chem.* **184,** 56 (1929).
[11] J. H. Northrop: *Jour. Gen. Physiol.* **1,** 607 (1919); **3,** 211 (1920); **5,** 263 (1922).
[12] L. Hugounenq and J. Loiseleur: *Bull. soc. chim. biol.* **7,** 955 (1925).
[13] R. Willstätter, W. Grassmann, and O. Ambros: *Zeit. physiol. Chem.* **151,** 307 (1925).
[14] E. Waldschmidt-Leitz and A. Purr: *Berichte* **62,** 2217 (1929).
[15] H. v. Euler and K. Josephson: *Zeits. physiol Chem.* **157,** 122 (1926). E. Waldschmidt-Leitz, W. Grassmann, and A. Schäffner: *Berichte* **60,** 359 (1927).
[16] E. Waldschmidt-Leitz, A. K. Balls, and J. Waldschmidt-Graser: *Berichte* 62, 956 (1929).
[17] J. H. Northrop: *Jour. Gen. Physiol.* **13,** 739 (1930).
[18] Wohlgemuth and Sugiwara: *Biochem. Zeits.* **163** (1925).
[19] E. Waldschmidt-Leitz and A. K. Balls: *Berichte* **63,** 1203 (1930).
[20] A. K. Balls and F. Köhler: *Ibid.* **64,** 383 (1931).
[21] E. Fischer: *Zeits. physiol. Chem.* **26,** 60 (1898).
[22] E. Abderhalden: *Wiener med. Wochenschrift* no. 1 (1930).
[23] H. v. Euler and K. Josephson: *Zeits. physiol. Chem.* **133,** 279 (1923).
[24] A. K. Balls: Habilitationsschrift, Prag 1930.
[25] M. Bergmann, V. DuVigneaud, and L. Zervas: *Berichte* **62,** 1909 (1929).
[26] A. K. Balls and F. Köhler: *Ibid.* **64,** 34 (1931).
[27] A. K. Balls and F. Köhler: *Ibid.* **64,** 294 (1931).
[28] E. Stiasny and H. Scotti: *Ibid.* **63,** 2977 (1930).

REPORT OF COMMITTEE ON RESEARCH GRANTS

A meeting of the Committee on Research Grants was held in the Research Laboratory of the General Electric Company, Schenectady, N. Y., at 9 A.M., Saturday, June 6, 1931. Present were Dr. W. R. Whitney, of the General Electric Company, Professor Harlow Shapley, Harvard University, and Professor Gary N. Calkins, Columbia University. By direction of the Executive Committee of the Society, the Committee on Award of Research Grants was authorized to distribute a sum not to exceed $3500 for the academic year 1931–32.

There were twenty applications for grants. All of the proposed projects were so important and the applicants so competent to carry on the work, that the committee found itself facing no easy task to distribute the available fund. After careful consideration, the following awards were made. The names are arranged alphabetically, and no significance is to be attached to the order of arrangement.

Charles Ernest Brown, $200. Position: Assistant Professor of Organic Chemistry, University of Vermont. Project: Relationship between chemical constitution and hypo-glycemic action in substituted guanidine types.

F. E. Chidester, $500. Position: Professor of Zoölogy, West Virginia University. Project: Nutrition and the endocrine glands.

Charles L. Fluke, Jr., $400. Position: Associate Professor in Economic Entomology, University of Wisconsin. Project: A revision of the species of the genus Syrphus (Syrphidæ Diptera) occurring in North America.

Mildred Hebel, $250. Position: Teaching Fellow, University of Tennessee. Project: Study of the order of plants known as the Papaverales of East Tennessee, with special reference to the Mustard family.

Rachel Emilie Hoffstadt, $250. Position: Assistant Professor of Bacteriology, University of Washington. Project: Continuation of study on mechanism of infection and local immunity.

Claude R. Kellogg, $500. Position: Professor of Biology, Fukien Christian University, Foochow, China. Project: Preparation of monograph on Chinese honey bee (Apis indica). (This work will be done at Johns Hopkins University during 1931–32 on bees which Professor Kellogg has personally brought from China.)

Thomas Large, $250. Position: Instructor in Zoölogy, Lewis and Clark High School, Spokane, Washington. Project: Study of fish fauna and their food and habits with particular attention to spawning of anadromous fishes.

Ann Haven Morgan, $300. Position: Professor of Zoölogy, Mount Holyoke College. Project: Studies of winter conditions of animals, especially aquatic invertebrates.

Alexander Petrunkevitch, $250. Position: Professor of Zoölogy, Yale University. Project: Structure, development, and activities of Hypochilus thorelli, the only spider of the sub-order Arachuomorphæ possessing four lungs and found in Tennessee and Georgia.

Richard Stephen Uhrbrock, $300. Position: Head, Statistical and Research Department, Industrial Relations Division, Proctor and Gamble Co., Cincinnati. Project: Statistical study of racial and sex differences in finger print patterns.

Paul Weatherwax, $300. Position: Associate Professor of Botany, Indiana University. Project: Study on phylogeny of the grass family, especially that of the Indian corn plant.

Reports from holders of grants for 1930–31 were received. They will be abstracted and presented in the December issue of the QUARTERLY.

The committee adjourned at 12:45 P.M.

W. R. WHITNEY
HARLOW SHAPLEY
GARY N. CALKINS

LIST OF MISSING PERSONS

Can You Help Us Locate These Members?

Name	*Chapter*	*Last Known Address*
Danielson, Florence Harris	Brown 1910	12 Prentiss St., Cambridge, Mass.
Dann, Walter M.	Ohio 1920	901 Center St., Wilkinsburg, Pa.
Danziger, Joseph L.	Columbia 1903	454 Fort Washington Ave., New York City
Dargan, William Hicklin	Iowa 1924	Univ. of Iowa, Iowa City, Iowa
Darling, Lewis Andrew	Stanford 1904 Cornell 1907	6310 N. 21st St., Philadelphia, Pa.
Darlington, Philip Jackson	Cornell 1891	60 W. Cedar St., Boston, Mass.
Darnell, Douglas L.	Case 1913	1687 Delmont Rd., East Cleveland, Ohio
Daugherty, Nathan Washington	Cornell 1913	
Dautel, Lee	Case 1921	
Davidman, Anna	Missouri 1921	9379 Evans, St. Louis, Mo.
Davidson, Godfrey Joseph	Worcester 1923	32 Carroll St., Worcester, Mass.
Davidson, Lloyd Booth	Iowa 1912	34 Grafton St., Arlington, Mass.
Davidson, Paul B.	Columbia 1923	
Davis, Arthur Cayley	Chicago 1921	Pacific Fleet, U. S. Navy (c/o Postmaster at San Francisco, Calif.)
Davis, Esther	Chicago 1923	2656 E. 74th St., Chicago, Ill.
Davis, Frank Wilson	Neb. 1924	International Combustion Engr. Corp., 200 Madison Avenue, New York City
Davis, John Henry, Jr. (Prof.)	Chicago 1928	Davidson College, Davidson, N. C.
Davis, Luther Dent	Purdue 1925	413 University St., W. Lafayette, Ind.
Davis, Marguerite	Chicago 1916	Univ. of Wisconsin, Madison, Wis.
Davis, Robert Leland	Mich. 1919	Queen's Univ., Kingston, Ont., Canada
Davis, Ruth Magdaline	U. of Wash. 1921	
Davis, Vernon Hayes	Ohio 1901	Ohio State University, Columbus, Ohio
Davis, W. H. (Dr.)	Wis. 1921	Dept. of Botany, Mass. Agri. College, Amherst, Mass.
Dawson, Morton Henry	McGill 1923	Royal Victoria Hospital, Pine Ave. W., Montreal, P. Q., Canada
Day, Lucy May	Cornell 1912	Clark University, Worcester, Mass.
Day, Warren French	Neb. 1906	City Engineer, Lincoln, Nebr.

Day, William Asher	Cornell 1886	112 W. Adams St., Chicago, Ill.
Dcheuneman, George D.	Ohio 1921	19 North Ohio Ave., Sidney, Ohio
Deacon, Frederick Sidney	Penn. 1914	241 Melville Ave., Philadelphia, Pa.
Dean, Dorothy	Chicago 1928	Charlevoix, Mich.
Dean, Walter Clark	Mich. 1922	7712 Brashear St., Pittsburgh, Pa.
De Camp, Lucille	Neb. 1925	1619 "R" Street, Lincoln, Nebr.
Decker, Carl Henry	Columbia 1904	c/o Forminiere, Dundu, Portuguese West Africa
De Eds, Floyd (Prof.)	Stanford 1923	Hygienic Laboratory, Washington, D. C.
De Eds, Mrs. Floyd	Stanford 1922	Hygienic Laboratory, Washington, D. C.
De Forest, Nora Stanton Blatch	Cornell 1905	
DeGray, Richard J.	Lehigh 1929	c/o Chemistry Dept., Lehigh Univ., Bethlehem, Pa.
Deiser, Norman A.	Columbia	296 Fenimon St., Brooklyn, N. Y.
Dekker, Dirk	Iowa State College 1926	General Delivery, Gary, Indiana
De Kruif, Paul Henry	Mich. 1914	Rockefeller Inst., New York City
Delprat, Dr. Guillaume D., Jr.	Calif. 1921 Calif. 1922	2633 Piedmont Ave., Berkeley, Calif.
De Meritt, Margaret	Washington 1913	
Deming, Jean Marjorie	Calif. 1924	2711 Virginia St., Berkeley, Calif.
Dennis, Leon C.	Missouri	477 Willoughby Ave., Brooklyn, N. Y.
Dennison, David Mathias	Mich. 1922	Univ. of Copenhagen, Copenhagen, Denmark
Dentith, F. W. H.	McGill 1925	
De Sou a, Jose Cuba	Union 1916	Caixa Postal 1098, São Paulo, Brazil
de Souza, Moacyr Alves	Cornell 1920	c/o Minister of Agriculture, Nova Scotia, Canada
de Villiers, Francois J.	Cornell 1924	Cornell Univ., Ithaca, N. Y.
Devine, Mervin Francis	Ohio 1923	1895 Belmore Rd., East Cleveland, Ohio
De Vore, R. W.	Purdue 1920	33 Pacific Ave., La Salle, N. Y.
Dewell, Henry Dirvendorf	Calif. 1906	1400 Scenic Ave., Berkeley, Calif.
Dewey, Albert Haskin (Prof.)	U. of Wash. 1909 Purdue 1914	Northern Pacific College of Pharmacy, Portland, Oregon
Diamond, Helen V.	Neb. 1922	1146 "K" St., Reedley, Calif.
Dick, Donald Edward	Idaho 1926	Lewiston, Idaho
Dick, George F.	Chicago 1910	Univ. of Chicago, Chicago, Ill.
Dickenson, Ernest H.	Columbia 1911	

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University of California at Davis.....	T. I. Storer....	.....	E. L. Proebsting	E. L. Proebsting
University of Utah.....	Elton Quinn...	I. B. Burns....	T. C. Adams...	.....
Clark University..	R. H. Goddard.	.....	O. W. Richards	O. W. Richards
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Duke Univ...	G. T. Hargitt..	W. C. Vosburgh	F. A. Wolf.....	F. A. Wolf
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